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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,221	02/24/2004	Avi Ashkenazi	P1216R1C1D6	1238

9157 7590 06/02/2006

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/785,221	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/7/04&4/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *attachment I*.

DETAILED ACTION

1. Claims 49-63 are pending and under examination in the instant application.

2. According to the priority statement of 2/24/04, Applicant claims priority to U.S.-provisional application 60,066, 364,PCT applications no. PCT/US98/24855 and PCT/US98/19437 and U.S. applications 09/953,499 and 09/254,465. Based on information given by applicant and an inspection of the patent applications, the examiner has concluded that the subject matter defined in this application is supported by the disclosure in U.S. Patent Applications 09/953,499, filed 9/14/2001 and 09/254,465, filed 3/5/1999; and PCT application PCT/US98/24855 (published as WO-9927098) filed 11/20/1998 but not supported by the others, for the following reasons: U.S provisional 60/066,364 does not disclose the amino acid sequence of PRO245. PCT/US98/19437 filed 9/17/1998, discloses the DNA and the amino acid sequence of PRO245. However, only the three priority applications listed above disclose an enabled use for PRO245, namely, that it inhibits VEGF stimulated proliferation of endothelial cells or induces apoptosis in endothelial cells. Accordingly, the subject matter defined in claims 49-59 has an effective filing date of 11/20/1998.

Should the applicant disagree with the Examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to 11/20/1998 which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession and fully enabled of prior to 11/20/1998.

3. The specification on page 1 should be amended to reflect the status of parent application No. 09/953,499 and 09/254,465.

4. Applicant's IDS, filed 6/7/04 and 4/18/05, is acknowledged. Only the references initiated were found in the parent applications 09/953,499 and 09/254,465. The BLAST results provided as reference Nos. 15-17 are not appropriate for an IDS. BLAST alignments should be appended as part of each individual sequence reference, which must include the Accession No., Database and earliest available date of the reference sequence in order to be appropriate for inclusion in the IDS.

5. There is a discrepancy in the length of SEQ ID NO: 11. Figure 5 shows that SEQ ID NO: 11 is a 1842 nucleotide sequence. The sequence listing indicates that SEQ ID NO:11 is a 2181 nucleotide sequence. Further, the specification on page 49, lines 36-40, discloses that clone DNA40628 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 52-54 (FIG. 5; SEQ ID NO: 11). The sequence listing SEQ ID NO:11 does not correspond with the translation initiation site at nucleotide positions 52-54. Clarification is required.

6. The specification is objected to for failing to provide a brief description of each individual Figure. Figure 1 has panels labeled A and B that must be identified in the Brief Description of the Drawings as "Figures 1A and 1B", after which each individual panel must be separately described. Similarly, figures 9 and 10. Correction is required.

7. The amendment to the specification on page 68, filed 2/24/04, to assure that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent", is sufficient to satisfy the deposit of the plasmid DNA35638-1141containting the cDNA encoding the polypeptide of SEQ ID NO: 9 (ATCC accession number 209265) under 35 U.S.C. § 112, first paragraph.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 53, 58 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 53, 58, and 63 are indefinite in the recitation of "PRO245" because its characteristics are not known. The use of "PRO245" polypeptide as the sole means of identifying the claimed polypeptide renders the claim indefinite because "PRO245" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation to define completely distinct polypeptide. It is suggested that the SEQ ID NO: 9 be cited in the claims.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 49-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "having at least 95% sequence identity" claimed in claim 49, line 1, represents a departure from the specification and the claims as originally filed.

Applicant's amendment filed 2/24/04 points to the specification on page 8, lines 14-31, page 11, lines 33-39, page 12, lines 9-10 & 24-33, page 13 line 4 to page 14 line 22 and pages 51-53 for

support for the newly added limitations "having at least 95% sequence identity" as claimed in claim 49. However, the specification does not provide a clear support of this limitation. The instant claims now recite limitations, which were not clearly disclosed in the specification and recited in the claims as originally filed.

12. Claims 49-63 are rejected under 35 U.S.C 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid having (a) the nucleotide sequence encoding the polypeptide of SEQ ID NO:9, (b) the nucleic acid sequence of SEQ ID NO: 8, (c) the full-length coding sequence of SEQ ID NO: 8 or the cDNA deposited under ATCC accession number 209265, a vector comprising the nucleic acid molecule, a host cell comprising the vector and a process for producing the PRO245 polypeptide of SEQ ID NO: 9, wherein PRO245 has the ability to inhibit of VEGF stimulated proliferation of endothelial cells, does not reasonably provide enablement for any isolated nucleic acid molecule "having at least 95% sequence identity" to: 49(a-e), or an isolated nucleic acid molecule comprising (b) a nucleotide sequence encoding the polypeptide of SEQ ID NO: 9 "lacking its associated signal sequence" in claim 54(a) or an isolated nucleic acid molecule that hybridizes under stringent conditions to 59(a-e). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The claims are directed to isolated nucleic acids having at least 95% sequence identity to SEQ ID NO: 8, a nucleotide sequence encoding the polypeptide of SEQ ID NO:8 with or without its signal peptide. Further the claims are directed to a nucleic acid molecule that hybridizes under specific stringent conditions to SEQ ID NO: 1 encoding SEQ ID NO:11 with or without the signal sequence. Dependent claims are directed to vectors, host cells comprising the isolated nucleic acids and process of producing the polypeptide.

The claimed nucleic acids are described at least in part in terms of the protein that might be encoded, the scope of the protein itself must be considered: The specification discloses that PRO245 has significant homology to both A33 antigen and JAM (see pp. 19, lines 37-38). Further the specification, on page 12, lines 9-10 discloses that the PRO245 polypeptide is 312 amino acids long. The specification on page 53, under example 4, discloses the use of the protein of SEQ ID NO:9 in the inhibition of VEGF stimulated proliferation of endothelial cells growth.

There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various nucleic acids recited in the instant claims. The art

recognizes that there is great functional diversity among proteins in this class, and that the functions are not yet well known. Tsukita *et al* (Nat Rev Mol Cell Biol. 2(4):285-293, 2001) teach the multifunctional strands in tight junction and that JAM was shown to be involved in cell-cell adhesion/junctional assembly of epithelial/endothelial cells as well as in the extravasation of monocytes through endothelial cells, but our knowledge on its function is still fragmentary (see page 287, 1st col., 2nd ¶). Tsukita *et al* concluded that the picture of the molecular architecture of tight junctions remains incomplete, and other important constituents need to be identified. Further development of the molecular biology of tight junctions will lead to a better understanding of their functions, not only in normal physiology, but also in disease (page 292, last ¶). Therefore, knowledge of one JAM's structure and function does not provide predictability about function of a structurally related JAM, even within the same class. There are great diversity and uncertainty of function. Without detailed direction as to which nucleic acid sequences are essential to the function of the encoded polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of nucleic acid sequences encompassed by the instant claims would share the ability to inhibit VEGF stimulated proliferation of EC of the encoded polypeptide of SEQ ID NO:9, other than the nucleic acid of SEQ ID NO:8 encoding SEQ ID NO:9.

Also, at issue is whether claimed SEQ ID NO: 9 would have an associated signal peptide or not as claimed in claims 49(b)-54(b), 56. The specification fails to locate the signal peptide cleavage site. Palmeri *et al* (J Biol Chem. 2000 Jun 23;275(25):19139-45) teaches that VE-JAM (claimed SEQ ID NO: 9) is highly localized to the intercellular boundaries of endothelial cells (see abstract). The skilled in the art would conclude that VE-JAM is not a secreted protein and therefore would not contain the secretion signal peptide.

The claims encompass an unreasonable number of inoperative polynucleotides, which the skilled artisan would not know how to use. There are no working examples of nucleic acids less than 100% identical to SEQ ID NO:8. The specification fails to provide guidance for using polypeptides related to (i.e. at least 95% identity) but not identical to SEQ ID NO:9 that share the ability to inhibit VEGF stimulated proliferation of EC of the encoded polypeptide of SEQ ID NO:9. The claims are broad because they do not require the claimed nucleic acid to encode a polypeptide identical to the disclosed sequence and because the claims have no functional limitation.

The art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases and recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences.

Claim 59 recites nucleic acid molecules that hybridize to the recited sequences. The term "hybridize" or "hybridization" generically refers to a process in which a strand of nucleic acid joins or matches up with a complementary strand through the process of base pairing, wherein

the process is basically used to locate or identify DNAs encoding specific proteins. It is well established in the art that 15-20 bases have been considered sufficient to achieve this process. The breadth of the claims includes nucleic acids of as little as 10 nucleotides. With these points in mind, it is the Examiner's position that given the claims their broadest reasonable interpretation, this language reads on an infinite number of possible DNA sequences for which there is not sufficient enablement.

The Examples provided in the specification do not provide a representative number of different DNA sequences that would enable a representative number of the above discussed DNA sequences with assurances that they possess or encode proteins having the desired activity, or alternatively can be used as probes or primers for the purpose of amplifying or detecting the PRO245 gene. The mere recitation of this term, and the definitions provided do not serve as sufficient guidance to enable the breadth of the claims for the various DNA sequences claimed. See Ex parte Forman, 230 USPQ 546. Since the first paragraph of the statute under 35 U.S.C 112 requires that there must be an enabling disclosure to support the breadth of the claims, a review of the specification confirms that the scope of the various DNA sequences that are discussed above have not been enabled. There is but a single nucleic acid disclosed with reference to PRO245, SEQ ID NO: 8. In the absence of sufficient guidance, it would require undue experimentation to enable a commensurate number of the sequences that are encompassed by the claims.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited nucleic acid sequence is unpredictable, as is the identity of which subsequences would hybridize to SEQ ID NO:8 encoding SEQ ID NO: 9 with or without signal sequence; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

13. Claims 49-63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an isolated nucleic acid having (a) the nucleotide sequence encoding the polypeptide of SEQ ID NO:9, (b) the nucleic acid sequence of SEQ ID NO: 8, (c) the full-length coding sequence of SEQ ID NO: 8 or the cDNA deposited under ATCC accession number 209265, a vector comprising the nucleic acid molecule, a host cell comprising the vector and a process for producing the PRO245 polypeptide of SEQ ID NO: 9, wherein PRO245 has the ability to inhibit of VEGF stimulated proliferation of endothelial cells.

Applicant is not in possession of any isolated nucleic acid molecule "having at least 95% sequence identity" to: 49(a-e), or an isolated nucleic acid molecule comprising (b) a nucleotide sequence encoding the polypeptide of SEQ ID NO: 9 "lacking its associated signal sequence" in

claim 54(a) or an isolated nucleic acid molecule that hybridizes under stringent conditions to 59(a-e).

Applicant has disclosed only nucleic acid of SEQ ID NO: 8 encoding SEQ ID NO:9 and a nucleotide sequence encoding the polypeptide of SEQ ID NO:9; therefore, the skilled artisan cannot envision all the contemplated nucleic acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claim 59 is rejected under 35 U.S.C. 102(b) as being anticipated by Bonaldo et al Genome Res. 6(9): 791-806 (1996).

Bonaldo et al teach a 753 nucleic acid molecule comprising a nucleic acid that is 100% identical to nucleic acids 1-661 of SEQ ID NO: 8,that would hybridize under stringent conditions to a complement of a nucleic acid molecule encoding the polypeptide of SEQ ID NO:6 with or without the single sequence, a complement of the nucleic acid sequence of SEQ ID NO: 8, a complement of the full-length coding sequence of the nucleic acids sequence of SEQ ID NO: 8 or, a complement of the full-length coding sequence of the cDNA deposited under ATCC accession number 209265 (see attached sequence alignment in particular).

The reference teachings anticipate the claimed invention.

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 60-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaldo et al Genome Res. 6(9): 791-806 (1996) in view of Darnell *et al.*

The teachings of Bonaldo et al have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of a host cell (claim 60) wherein the host cell is a CHO cell an *E. coli* a yeast cell or a Baculvirus-infected insect cell (claim 62), a vector (claim 60) and a method for producing a polypeptide (claim 63).

Darnell et al teach that in order to prepare an unlimited amount of a pure gene, a vector containing the gene can be grown in a host cell and DNA extracted. Darnell *et al* also teach an expression vector in order to take advantage of "bacterial tricks" that increase mRNA synthesis to produce large quantities of desired proteins using a eukaryotic vector and host cell, or a prokaryotic and bacterial vector and host cell (page 255-258 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to express the DNA taught by the Bonaldo et al using the vectors, host cells and the method of producing the polypeptide as taught by Darnell *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because a vector containing the a gene that grown in a host cell offers to prepare an unlimited amount of a pure gene as well as to produce large quantities of desired proteins as taught by Darnell *et al.*

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 23, 2006

Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600

attachment I

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Qy        421 TAGTGCCCCATCTGAGCAAGGCCAAAACCTGGAAGAGGATACAGTCACTCTGGAAGTATT 480
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REFERENCE   1  (bases 1 to 681)
  AUTHORS   NIH-MGC http://mgc.nci.nih.gov/.
  TITLE     National Institutes of Health, Mammalian Gene Collection (MGC)
  JOURNAL   Unpublished (1999)
COMMENT     Contact: Robert Strausberg, Ph.D.
            Email: cgapbs-r@mail.nih.gov
            Tissue Procurement: Life Technologies, Inc.
             cDNA Library Preparation: Life Technologies, Inc.
             cDNA Library Arrayed by: The I.M.A.G.E. Consortium (LLNL)
             DNA Sequencing by: Incyte Genomics, Inc.
             Clone distribution: MGC clone distribution information can be
            found through the I.M.A.G.E. Consortium/LLNL at:
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                     Site_2: EcoRV (destroyed); RNA source anonymous pool of 3
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                     and male age 26 weeks.  Library is oligo-dT primed and
                     directionally cloned (EcoRV site is destroyed  upon
                     cloning).  Average insert size 1.7 kb, insert size range
                     0.7-3.5 kb.  Library is normalized and enriched for
                     full-length clones and  was constructed by C. Gruber
                     (Invitrogen).  Research Genetics  tracking code 017. Note:
                     this is a NIH_MGC Library."
ORIGIN

  Query Match             48.5%;  Score 628;  DB 2;  Length 681;
  Best Local Similarity   99.9%;  Pred. No. 6.9e-299;
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Qy        301 CTTTGTCTACTATCAACAGACTCTTCAAGGTGATTTTAAAAATCGAGCTGAGATGATAGA 360
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Db        301 CTTTGTCTACTATCAACAGACTCTTCAAGGTGATTTTAAAAATCGAGCTGAGATGATAGA 360

Qy        361 TTTCAATATCCGGATCAAAAATGTGACAAGAAGTGATGCGGGGAAATATCGTTGTGAAGT 420
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Db        361 TTTCAATATCCGGATCAAAAATGTGACAAGAAGTGATGCGGGGAAATATCGTTGTGAAGT 420

Qy        421 TAGTGCCCCATCTGAGCAAGGCCAAAACCTGGAAGAGGATACAGTCACTCTGGAAGTATT 480
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Qy        481 AGTGGCTCCAGCAGTTCCATCATGTGAAGTACCCTCTTCTGCTCTGAGTGGAACTGTGGT 540
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Qy        541 AGAGCTACGATGTCAAGACAAAGAAGGGAATCCAGCTCCTGAATACACATGGTTTAAGGA 600
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Db        541 AGAGCTACGATGTCAAGACAAAGAAGGGAATCCAGCTCCTGAATACACATGGTTTAAGGA 600

Qy        601 TGGCATCCGTTTGCTAGAAAATCCCAGACTTGGCTCCCAAAGCACCAACAGCTCATACAC 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 TGGCATCCGTTTGCTAGAAAATCCCAGACTTGGCTCCCAAAGCACCAACAGCTCATACAC 660

Qy        661 AATGAATACAAAAACTGGA 679
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Db        661 AATGAATACAAAAACTGGA 679
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RESULT 11
CF127652
LOCUS       CF127652                753 bp    mRNA    linear   EST 05-AUG-2003
DEFINITION  UI-HF-ET0-awi-a-14-0-UI.r1 NIH_MGC_214 Homo sapiens cDNA clone
            IMAGE:30552877 5', mRNA sequence.
ACCESSION   CF127652
VERSION     CF127652.1  GI:33206105
KEYWORDS    EST.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (bases 1 to 753)
  AUTHORS   Bonaldo,M.F., Lennon,G. and Soares,M.B.
  TITLE     Normalization and subtraction: two approaches to facilitate gene
            discovery
  JOURNAL   Genome Res. 6 (9), 791-806 (1996)
   PUBMED   8889548
COMMENT     Contact: Soares, MB
            Coordinated Laboratory for Computational Genomics
            University of Iowa
            375 Newton Road , 4156  MEBRF, Iowa City, IA 52242, USA
            Tel: 319 335 8250
            Fax: 319 335 9565
            Email: bento-soares@uiowa.edu
            Tissue Procurement: Mary Hendrix
```

cDNA Library preparation: Dr. M. Bento Soares, University of Iowa
cDNA Library Arrayed by: Dr. M. Bento Soares, University of Iowa
DNA Sequencing by: Dr. M. Bento Soares, University of Iowa
Clone Distribution: Distribution information can be found at
http://genome.uiowa.edu/distribution/humanfl.html
Seq primer: pYX-5.

FEATURES Location/Qualifiers
source 1. .753
/organism="Homo sapiens"
/mol_type="mRNA"
/db_xref="taxon:9606"
/clone="IMAGE:30552877"
/tissue_type="Chondrosarcoma Lung Metastasis cell lines"
/lab_host="DH10B (T1 phage resistant)"
/clone_lib="NIH_MGC_214"
/note="Organ: Lung; Vector: pYX-Asc; Site_1: EcoR I; Site_2: Not I; The library was constructed according Bonaldo, Lennon and Soares, Genome Research, 6:791-806, 1996. Denatured RNA was size fractionated on a 1% agarose gel. First strand cDNA synthesis was primed with oligo-dT primer containing a Not I site. Double strand cDNA was size selected according to mRNA size fraction, ligated with EcoR I adaptor, digested with Not I and then cloned directionally into pYX-Asc vector. The library tag sequence located between the Not I site and the polyA tail is GATAAGGCCA. Tissue was provided by Mary Hendrix."

ORIGIN

Query Match 47.6%; Score 616; DB 5; Length 753;
Best Local Similarity 100.0%; Pred. No. 6e-293;
Matches 616; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 CCCAGAAGTTCAAGGGCCCCCGGCCTCCTGCGCTCCTGCCGCCGGGACCCTCGACCTCCT 60
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Db        138 CCCAGAAGTTCAAGGGCCCCCGGCCTCCTGCGCTCCTGCCGCCGGGACCCTCGACCTCCT 197

Qy         61 CAGAGCAGCCGGCTGCCGCCCCCGGGAAGATGGCGAGGAGGAGCCGCCACCGCCTCCTCCT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        198 CAGAGCAGCCGGCTGCCGCCCCGGGAAGATGGCGAGGAGGAGCCGCCACCGCCTCCTCCT 257

Qy        121 GCTGCTGCTGCGCTACCTGGTGGTCGCCCTGGGCTATCATAAGGCCTATGGGTTTTCTGC 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        258 GCTGCTGCTGCGCTACCTGGTGGTCGCCCTGGGCTATCATAAGGCCTATGGGTTTTCTGC 317

Qy        181 CCCAAAAGACCAACAAGTAGTCACAGCAGTAGAGTACCAAGAGGCTATTTTAGCCTGCAA 240
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Db        318 CCCAAAAGACCAACAAGTAGTCACAGCAGTAGAGTACCAAGAGGCTATTTTAGCCTGCAA 377

Qy        241 AACCCCAAAGAAGACTGTTTCCTCCAGATTAGAGTGGAAGAAACTGGGTCGGAGTGTCTC 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        301 CTTTGTCTACTATCAACAGACTCTTCAAGGTGATTTTAAAAATCGAGCTGAGATGATAGA 360
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Qy        541 AGAGCTACGATGTCAAGACAAAGAAGGGAATCCAGCTCCTGAATACACATGGTTTAAGGA 600
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Db        678 AGAGCTACGATGTCAAGACAAAGAAGGGAATCCAGCTCCTGAATACACATGGTTTAAGGA 737

Qy        601 TGGCATCCGTTTGCTA 616
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Db        738 TGGCATCCGTTTGCTA 753
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RESULT 12
DB289885
LOCUS DB289885 587 bp mRNA linear EST 11-DEC-2005
DEFINITION DB289885 UTERU3 Homo sapiens cDNA clone UTERU3019733 5', mRNA sequence.
ACCESSION DB289885
VERSION DB289885.1 GI:83558149
KEYWORDS EST.
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 587)
AUTHORS Kimura,K., Wakamatsu,A., Suzuki,Y., Ota,T., Nishikawa,T., Yamashita,R., Yamamoto,J., Sekine,M., Tsuritani,K., Wakaguri,H., Ishii,S., Sugiyama,T., Saito,K., Isono,Y., Irie,R., Kushida,N., Yoneyama,T., Otsuka,R., Kanda,K., Yokoi,T., Kondo,H., Wagatsuma,M., Murakawa,K., Ishida,S., Ishibashi,T., Takahashi-Fujii,A., Tanase,T., Nagai,K., Kikuchi,H., Nakai,K., Isogai,T. and Sugano,S.
TITLE Diversification of Transcriptional Modulation: Large-scale Identification and Characterization of Putative Alternative Promoters of Human Genes
JOURNAL Genome Res. 16 (1), 55-65 (2006)
PUBMED 16344560
COMMENT Contact: Takao Isogai
FLJ Project (HRI Team)
Helix Research Institute
2-6-7 Kazusa-Kamatari, Kisarazu, Chiba, 292-0818, Japan
Tel: 81-438-52-3975
Fax: 81-438-52-3986
Email: flj-cdna@nifty.com
NEDO human cDNA project (New Energy and Industrial Technology Developmental Organization, Japan); cDNA library construction: Helix Research Institute (HRI); 5'-end one pass sequencing: HRI, Research Association for Biotechnology (RAB) and Biotechnology Center, National Institute of Technology and Evaluation; 3'-end one pass sequencing: RAB.

FEATURES Location/Qualifiers
source 1. .587
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/mol_type="mRNA"
/db_xref="taxon:9606"
/clone="UTERU3019733"
/tissue_type="uterus"
/clone_lib="UTERU3"
/note="Vector: pME18SFL3"

ORIGIN

Query Match 45.3%; Score 587; DB 9; Length 587;
Best Local Similarity 100.0%; Pred. No. 1.3e-278;
Matches 587; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          4 AGAAGTTCAAGGGCCCCCGGCCTCCTGCGCTCCTGCCGCCGGGACCCTCGACCTCCTCAG 63
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Qy         64 AGCAGCCGGCTGCCGCCCCGGGAAGATGGCGAGGAGGAGCCGCCACCGCCTCCTCCTGCT 123
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 AGCAGCCGGCTGCCGCCCCGGGAAGATGGCGAGGAGGAGCCGCCACCGCCTCCTCCTGCT 120

Qy        124 GCTGCTGCGCTACCTGGTGGTCGCCCTGGGCTATCATAAGGCCTATGGGTTTTCTGCCCC 183
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GCTGCTGCGCTACCTGGTGGTCGCCCTGGGCTATCATAAGGCCTATGGGTTTTCTGCCCC 180

Qy        184 AAAAGACCAACAAGTAGTCACAGCAGTAGAGTACCAAGAGGCTATTTTAGCCTGCAAAAC 243
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 AAAAGACCAACAAGTAGTCACAGCAGTAGAGTACCAAGAGGCTATTTTAGCCTGCAAAAC 240
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